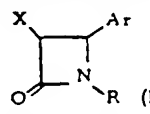
84325 D/46 B03 SAGA 07.03.80
SAGAMI CHEM RES CENTRE *J5 6125-360
07.03.80-JP-028057 (01.10.81) C07d-205/08 C07d-401/04 C07d-403/04 C07d-405/04 C07d-407/04 C07d-409/04

Growth regulator intermediate beta-lactam cpds. - convertible into alpha oxyacid amide(s) or alpha aminoacid amide(s)

B(7-D1). 1

β-Lactam cpds. of formula (I) are new:



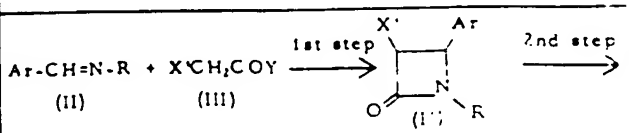
(I)

(Ar = heteroaromatic gp. or substd. phenyl of formula p-Y-C$_6$H$_4$-;
Y = F, OH or protected OH;
R = alkyl, aryl or heteroaromatic gp;
X = amino, azido, benzyloxy or OH;
provided that when X = azido, Ar is not p-fluorophenyl).

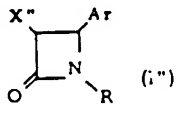
USE/ADVANTAGE

(I) on cleavage of the β-lactam ring can be converted into α-hydroxy acid amides or α-amino acid amides, e.g. tryptophan, tyrosine or p-fluorophenylalanine amides. p-Fluorophenylalanine amide is useful as a growth regulator for animals; other amino acid amides can be converted into physiologically active substances.

PREPARATION



(II) (III) (I')



(I")

(X' = benzyloxy or azido;
X" = OH or amino;
Z = halogen or OH;
provided that when X' = azido, Ar is not p-fluorophenyl).
1st step: The reaction is conducted in a solvent, e.g. PhH, PhMe, THF, CH_2Cl_2, in presence of a tertiary amine, e.g. Et_3N, Pr_3N, Bu_3N, pyridine, N-methylpiperidine, N-methylpyrrolidine, 1,8-di-azabicyclo [5.4.0]-7-undecene, at a temp. of -78 to 100°C.
2nd step: The reaction is achieved by hydrogenolysis with

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a catalyst, e.g. Pd black, Pd-C, in a solvent, e.g. MeOH, EtOH, CH_2Cl_2, $CHCl_3$, PhH, PhMe, THF, MeCN, DMF, at from room temp. to 150°C, pref. 50-100°C.

EXAMPLE

To a soln. of 4.00 g 2-furylmethylideneaniline and 3.07 g Et_3N in 50 ml PhH was dropwise added slowly a soln. of 5.61 g benzyloxyacetyl chloride in 50 ml PhH under ice cooling, and the mixt. was slowly warmed up to room temp., stirred for 15 hrs., then washed with water, dried on $MgSO_4$, and evapd. in vacuo to give 7.64 g yellow solid. This was chromatographed on a column of silica gel (Wako gel C-200) and eluted with n-hexane-EtOAc (9 : 1) to give cis-1-phenyl-3-benzyloxy-4-(2'-furyl)azetidin-2-one as white crystals, m.pt. 100-101°C, and the trans-isomer, as white crystals, m.pt. 115.5 - 117°C.(9ppW52).

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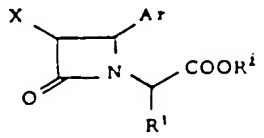
84326 D/46 B03 SAGA 07.03.80
SAGAMI CHEM RES CENTRE *J5 6125-361
07.03.80-JP-028059 (01.10.81) C07d-205/08

Azetidinone cpds. - which are cleavable to form physiologically active dipeptide(s)

B(7-D1) N(2-F1, 2-F2)

Azetidinone cpds. of formula (I) are new:



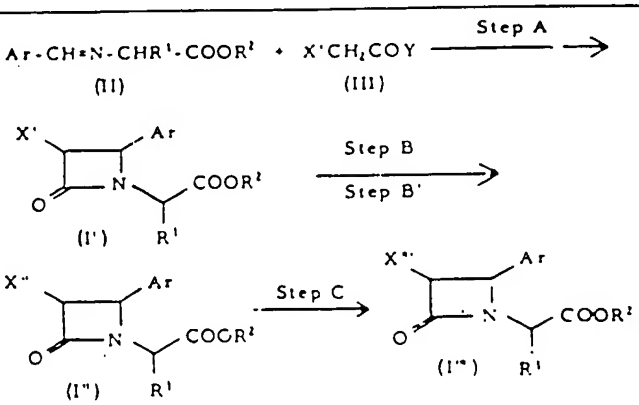
(I)

(Ar = aromatic gp.;
R^1 = H, alkyl or aryl;
R^2 = alkyl or aryl;
X = amino, acylamino, azido, benzyloxy or OH).

USE/ADVANTAGE

(I) on cleavage of the azetidinone ring can be converted into physiologically active dipeptides.

PREPARATION



(II) (III) (I') (I") (I"')

(X' = benzyloxy or azido;
X" = OH or amino;
X"' = acylamino;

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